Claims

1. A method of producing a mammalian cell capable of high efficiency packaging of a recombinant AAV (rAAV) vector, said method comprising the steps of:

(a) providing a mammalian cell which comprises a stably integrated AAV cap gene operably linked to a promoter, and a stably integrated AAV rep gene operably linked to a heterologous promoter;

(b) replicating the cell of step (a) to produce a population of cells;

(c) introducing a helper virus to the population of cells of step (b); and

(d) selecting a cell exhibiting helper-virus-inducible rep protein activity.

2. A method according to claim 1, wherein said helper virus is an adenovirus.

3. A method according to claim 1, wherein said packaging cell is capable of growing at least one half as rapidly as parental-type cells that do not contain an AAV rep gene, and wherein said packaging cell is capable of packaging rAAV vectors to produce at least 100 rAAV particles/cell.

4. A method according to claim 1, wherein said mammalian cell of step (a) comprises the combined rep and cap genes of AAV in which the p5 promoter has been replaced by a heterologous promoter.

5. A method according to claim 4, wherein said heterologous promoter is a mouse metallothionein I (mMT-I) promoter.

6. A cell produced by the method of claim 1, and progeny thereof.

7. A cell produced by the method of claim 3, and progeny thereof.

8. A cell produced by the method of claim 4, and progeny thereof.

9. A cell produced by the method of claim 5, and progeny thereof.

10. A mammalian cell capable of high efficiency packaging of a recombinant AAV (rAAV) vector, said cell comprising a stably integrated cap gene operably linked to a promoter, and a stably integrated rep gene operably linked to a heterologous promoter; wherein said cell exhibits helper-virus-inducible rep protein activity.

11. An AAV packaging cell of claim 10, wherein said helper-virus-inducible rep protein activity is inducible by adenovirus.

12. An AAV packaging cell of claim 10, wherein said packaging cell is capable of growing at least one half as rapidly as parental-type cells that do not contain an AAV rep gene, and wherein said packaging cell is capable of packaging rAAV vectors to produce at least 100 rAAV particles/cell.

13. An AAV packaging cell of claim 10, wherein said cell comprises the combined rep and cap genes of AAV in which the p5 promoter has been replaced by a heterologous promoter.

14. An AAV packaging cell of claim 13, wherein said heterologous promoter is a mouse metallothionein I (mMT-I) promoter.

15. An AAV packaging cell of claim 10, further comprising a stably integrated recombinant AAV vector, said

vector comprising a polynucleotide sequence of interest located between two AAV inverted terminal repeat (ITR) regions.

16. A method of packaging a recombinant AAV vector, comprising the steps of:

(a) providing an AAV packaging cell of claim 10;

(b) introducing a recombinant AAV vector, said vector comprising a polynucleotide sequence of interest located between two AAV inverted terminal repeat (ITR) regions;

(c) introducing a helper virus; and

(d) incubating the cell under conditions suitable for replication and packaging of AAV.

17. A method of packaging a recombinant AAV vector, comprising the steps of:

(a) providing an AAV packaging cell of claim 15 which comprises a stably integrated rAAV vector;

(b) introducing a helper virus; and

(c) incubating the cell under conditions suitable for replication and packaging of AAV.

18. A recombinant AAV vector packaged according to the method of claim 16.

19. A recombinant AAV vector packaged according to the method of claim 17.

20. A recombinant AAV vector of claim 19, wherein said vector comprises a polynucleotide encoding a cystic fibrosis transmembrane conductance regulator (CFTR).

21. A method of determining the relative infectious titer of an rAAV vector preparation, comprising the steps of:

(a) introducing a helper virus and serial dilutions of the rAAV vector preparation to AAV packaging cells of claim 10;

(b) incubating the cells under conditions suitable for replication of AAV; and

(c) determining the amount of replicated rAAV vector.